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 NEWS 24  Sep 16  Experimental properties added to the REGISTRY file
 NEWS 25  Sep 16  Indexing added to some pre-1967 records in CA/CAPLUS
 NEWS 26  Sep 16  CA Section Thesaurus available in CAPLUS and CA
 NEWS 27  Oct 01  CASREACT Enriched with Reactions from 1907 to 1985
 NEWS 28  Oct 21  EVENTLINE has been reloaded
 NEWS 29  Oct 24  BEILSTEIN adds new search fields
 NEWS 30  Oct 24  Nutraceuticals International (NUTRACEUT) now available on STN
 NEWS 31  Oct 25  MEDLINE SDI run of October 8, 2002
 NEWS 32  Nov 18  DKILIT has been renamed APOLLIT

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L2        12387 COX-2

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L3   ANSWER 1 OF 1  CA  COPYRIGHT 2002 ACS
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AN 135:102178 CA
TI Wogonin, baicalin, and baicalein inhibition of inducible nitric oxide synthase and cyclooxygenase-2 gene expressions induced by nitric oxide synthase inhibitors and lipopolysaccharide
AU Chen, Y.-C.; Shen, S.-C.; Chen, L.-G.; Lee, T. J.-F.; Yang, L.-L.
CS Graduate Institute of Pharmacognosy Science, Taipei Medical University, Taipei, Taiwan
SO Biochemical Pharmacology (2001), 61(11), 1417-1427
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L3 ANSWER 1 OF 1 CA
AB We previously reported that oroxylin A, a polyphenolic compound, was a potent inhibitor of lipopolysaccharide (LPS)-induced expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (**COX-2**). In the present study, three oroxylin A structurally related polyphenols isolated from the Chinese herb Huang Qui, namely baicalin, baicalein, and wogonin, were examined for their effects on LPS-induced nitric oxide (NO) production and iNOS and **COX-2** gene expressions in RAW 264.7 macrophages. The results indicated that these three polyphenolic compds. inhibited LPS-induced NO production in a concentration-dependent manner without a notable cytotoxic effect on these cells.
The decrease in NO production was in parallel with the inhibition by these polyphenolic compds. of LPS-induced iNOS gene expression. However, these three compds. did not directly affect iNOS enzyme activity. In addition, wogonin, but not baicalin or baicalein, inhibited LPS-induced prostaglandin E2 (PGE2) production and **COX-2** gene expression without affecting **COX-2** enzyme activity. Furthermore, N-nitro-l-arginine (NLA) and N-nitro-l-arginine Me ester (L-NAME) pretreatment enhanced LPS-induced iNOS (but not **COX-2**) protein expression, which was inhibited by these three polyphenolic compds. Wogonin, but not baicalin or baicalein, similarly inhibited PGE2 production and **COX-2** protein expression in NLA/LPS or L-NAME/LPS-co-treated RAW 264.7 cells. These results indicated that co-treatment with NOS inhibitors and polyphenolic compds. such as wogonin effectively blocks acute production of NO and, at the same time, inhibits expression of iNOS and **COX-2** genes.
AN 135:102178 CA
TI Wogonin, baicalin, and baicalein inhibition of inducible nitric oxide synthase and cyclooxygenase-2 gene expressions induced by nitric oxide synthase inhibitors and lipopolysaccharide
AU Chen, Y.-C.; Shen, S.-C.; Chen, L.-G.; Lee, T. J.-F.; Yang, L.-L.
CS Graduate Institute of Pharmacognosy Science, Taipei Medical University, Taipei, Taiwan
SO Biochemical Pharmacology (2001), 61(11), 1417-1427
CODEN: BCPCA6; ISSN: 0006-2952
PB Elsevier Science Inc.
DT Journal
LA English
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L3: Entry 4 of 4 File: USPT Jul 24, 2001

DOCUMENT-IDENTIFIER: US 6264995 B1
TITLE: Herbal composition for reducing inflammation and methods of using same

Abstract Text (1):
An herbal composition reducing inflammation in bones and joints by inhibiting the enzyme cyclooxygenase-2 is prepared from holy basil, turmeric, ginger, green tea, rosemary, huzhang, Chinese goldthread, barberry, oregano and scutellariae baicalensis. More particularly, the herbal composition of the present invention contains therapeutically effective amounts of the supercritical extracts of ginger, rosemary and oregano, and therapeutically effective amounts of extracts of holy basil, turmeric, green tea, huzhang, Chinese goldthread, barberry, rosemary and scutellariae baicalensis. The herbal composition can be administered orally, topically or parenterally. Particularly preferred embodiments are soft gel capsules for oral administration and creams for topical application. In addition to reducing inflammation, the herbal composition also promotes healthy joint function and, because it inhibits cyclooxygenase-2 (COX-2), the composition also promotes normal cell growth. Furthermore, the herbal composition contains organic anti-aging constituents that inactivate oxygen free radicals, thereby providing antioxidant benefits in addition to anti-inflammatory benefits.

Brief Summary Text (5):
There are two forms of the cyclooxygenase enzyme: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). The latter form, i.e., COX-2, appears to play a key role in inflammatory processes. Recent scientific studies suggest that inhibiting the COX-2 enzyme may be an effective wayto reduce inflammation without the side effects associated with irreversible COX-1 inhibition. In addition, recent scientific studies also suggest that COX-2 inhibition may serve an important function in promoting normal cell growth in the colon, pancreas, breast tissue and other organ systems.

Brief Summary Text (6):
Drugs are being developed which are intended to selectively inhibit COX-2 with minimal effect on COX-1. However, despite the emphasis on COX-2 inhibition, these drugs appear to have serious side effects, e.g., a breakdown in digestive protective mucus and prevention of normal healing processes. For example, non-steroidal anti-inflammatory drugs (NSAIDS) can have a variety of toxic side effects such as, e.g., gastric erosion and adverse effects on kidneys and liver, and may inadequately regulate the cellular immune functions and secretions of various cytokines.

Brief Summary Text (16):
According to various studies, ocimum sanctum (holy basil) possesses significat anti-inflammatory properties and is capable of blocking both the cyclooxygenase and lipoxygenase pathways of arachidonate metablism. See e.g., J. Ethnopharmacol. April 1999; 65(1);13-9, Evaluation of the Gastric Antiulcer Activity of Fixed Oil of Ocimun Sanctum (Holy Basil), Singh, S. Majundar DK College of Pharmacy, University of Delhi, India; Indian J. Exp. Biol. October 1998; 36(10): 1028-31, Comparative Evaluation of Antiinflammatory Potential of Fixed Oil of Different Species of Ocimun and Its Possible Mechanism of Action, Singh S. College of Pharmacy (University of Delhi), Pushp Vihar, India; J. Ethnopharmacol. October 1996; 54(1):19-26, and Evaluation of Anti-Inflammatory Potential of Fixed Oil of Ocimum Santum (Holy Basil) and Its Possible Mechanism of Action, Singh, S., Majunbar D K, Rehan H M College of Pharmacy (University of Delhi), New Delhi, India. The marker constituents of ocimum sanctum,

i.e., ursolic acid and oleanolic acid (less active) have been found to a significant COX-2 inhibitory effect. See, for example, Indian J. Exp. Biol. April 1997, 35(4):380-3, Evaluation of Antiinflammatory Activity of Fatty Acids of Ocinum Sanctum Fixed Oil, Singh S., Majumdar DK College of Pharmacy (University of Delhi) Pushp Vihar, New Delhi, India; and FEBS Lett. Mar. 16, 1992; 299(3):213-7, Characterization of Uroslic Acid as a Lipoxygenase and Cyclooxygenase Inhibitor Using Macrophages, Platelets and Differentiated HL60 Leukemic Cells, Najid A., Simon A., Cook J., Chable-Rabinovitch H., Delage C., Chulia A J, Rigaud M. CJF INSERM 88-03, Faculte de Medecine, Universite de Limoges, France; J. Nat. Prod. October 1998; 61(10); 1212-5, Ursolic Acid from Plantago Major, a Selective Inhibitor of Cyclooxygenase-2 Catalyzed Protaglandin Biosynthesis, Ringbom T., Segura L., Noreen Y., Perera P., Bohlin L. Divison of Pharmacognosy, Department of Pharmacy, Biomedical Centre, Uppsala University, Box 579, S-751 223 Uppsala, Sweden; Cancer Res. Feb. 15, 1998; 58(4):717-23 Novel Triterpenoids Suppress Inducible Nitric Oxide Synthase (iNOS) and Inducible Cyclooxygenase (COX-2) in Mouse Macrophages, Suh N., Honda T., Finlay H. J., Barchowsky A., Williams C., Benoit N. E., Xie Q. W., Nathan C., Gribble G. W., Sporn M. B., Department of Phamacology and Norris Cotton Cancer Center, Dartmouth Medical School, Hanover, N.H. 03755 USA; Indian J. Exp. Biol. December 1996; 34(12):1212-5, Chemical and Pharmacological Studies on Fixed Oil of Ocimun Sanctum; Singh S., Majumdar D. K., Yadov M. R., College of Pharmacy (University of Delhi) Pushp Vihar, India.; J. Ethnopharmacol November 1987, 21(2):153-63, Ocinum Sanction: An Experimental Study Evaluating Its Anti-Inflammatory, and Analgesic and Antipyretic Activity in Animals; Godhwani, S., Godhwani, J. L., Vyas D. S., Department of Phamacology and Experimental Therapeutics, Sandar Patel Medical College, Rajasthan, India.

Brief Summary Text (17):
Curcumin, a major principal of turmeric, has been found to directly inhibit the activity of COX-2. See, e.g., Carcinogenesis March 1999, 20(3):445-51, Curcumin Inhibits Cyclooxgenase-2 Transcription in Bile Acid- and Phorbol Ester-Treated Human Gastrointestinal Epithelial Cells, Zhang F., Altorki N. K., Mestre J. R., Subbaramiah K., Dannenberg A. J., Department of Cardiothoracic Surgery, New York Presbyterian Hospital and Weill Medical College of Cornell University, New York 10021, USA. See also, e.g., Agents Actions October 1982, 12(4):508-15, Anti-Inflammatory and Irritant Activities of Curcumin Analogues in Rats, Mukhopadhyay A., Basu N., Ghatak N., Gujral P. K; and Int J Clin Pharmacol Ther Toxicol December 1986, 24(12):651-4, Evaluation of Anti-Inflammatory Property of Curcumin (Diferuloyl Methxane) in Patients with Postoperative Inflammation, Satoskar R. R., Shah S. J., Shenoy S. G.

Brief Summary Text (18):
Melatonin, a constituent of ginger, has been found to exert potent anti-inflammatory effects via COX-2 inhibition. See, e.g., J Pineal Res August 1999, 27(1):9-14, Regulation of Prostaglandin Production in Carrageenan-Induced Pleurisy by Melatonin, Cuzzocrea S, Costantino G., Mazzon E., Caputi A. P., Institute of Pharmacology, School of Medicine, University of Messina, Italy; Biochem Mol Biol Int March 1995, 35(3):627-34, Identifacation of Melatonin in Plants and Its Effects on Plasma Melatonin Levels and Binding to Melatonin Receptors in Vertebrates, Hattori A., Migitaka H., Iigo M., Yamamoto K., Ohtani-Kaneko R., Hara M., Suzuki T., Reiter R. J., Department on Anatomy, St. Marianna University School of Medicine, Kawasaki, Japan. See also Biomed Biochim Acta 1984; 43(8-9):S335-46, Aqueous Extracts of Onion, Garlic and Ginger Inhibit Platelet Aggregation and Alter Arachidonic Acid Metabolism, Srivastava K. C.; and Cancer Res Mar. 1, 1996; 56(5):1023-30, Inhibition of Tumor Promotion in SENCAR Mouse Skin by Ethanol Extract of Zingiber Officinale Rhizome, Katiyar S. K., Agarwal R., Mukhtar H., Department of Dermatology, Skin Diseases Research Center, University Hospitals of Cleveland, Case Western Reserve University, Ohio.

Brief Summary Text (22):
In addition, a group of compounds identified as flavan-3-ol derivatives (+)-catechin, rich in green tea, have been identified as COX-1 and COX-2 inhibitors, See, e.g., Planta Med August 1998; 64(6):520-4 Flavan-3-ols isolated from some medicinal plants inhibiting COX-1 and COX-2 catalysed prostaglandin biosynthesis. Noreen Y., Serrano G, Perera P., Bohlin L Department of Pharmacy, Uppsala University, Sweden; J Nat Prod January 1998; 61(1):8-12 Two new isoflavones from Ceiba pentandra and their effect on cyclooxygenase-catalysed prostaglandin biosynthesis. Noreen Y., el-Seedi H, Perera P.,

Bohlin L Department of Pharmacy, Uppsala University, Sweden; J Nat Prod January 1998; 61(1):2-7 Development of a radiochemical cyclooxygenase-1 and -2 in vitro assay for identification of natural products as inhibitors of prostaglandin biosynthesis. Noreen Y., Ringbom T., Perera P., Danielson H, Bohlin L Department of Pharmacy, Uppsala University, Sweden.

Brief Summary Text (23):
Salicylic acid, another constituent of green tea, also has been found to be a COX-2 inhibitor. Reference is made, e.g., to Mol Pharmacol June 1997, 51(6):907-12, Sodium Salicylate Inhibits Cyclo-Oxygenase-2 Activity Independently of Transcription Factor (Nuclear Factor KappaB) Activation: Role of Adrachidonic Acid, Mitchell J. A., Saunders M., Barnes P. J., Newton R., Belvisi M. G., Department of Anaesthesia and Critical Care Medicine, The Royal Brompton Hospital, London, England.

Brief Summary Text (24):
Berberine, found in barberry and Chinese goldthread, has been found to inhibit COX-2 without inhibiting COX-1 activity. Reference is made, e.g., to J Ethnopharmacol August 1999; 66(2):227-33 Inhibition by berberine of cyclooxygenase-2 transcriptional activity in human colon cancer cells; Fukuda K, Hibiya Y, Mutoh M, Koshiji M, Akao S, Fujiwana H Department of Oriental Medicine, Gifu University School of Medicine, Japan; and Biol Pharm Bull August 1998; 21(8):814-7 Inhibitory effect of Coptidis Rhizoma and Scutellariae Radix on azoxymethane-induced aberrant crypt foci formation in rat colon. Fukutake M, Yokota S, Kawamura H, Iisuka A, Amagaya S, Fukuda K, Komatsu Y Central Research Laboratories, Tsumura & Co., Ibaraki, Japan.

Brief Summary Text (26):
Scutellaria baicalensis has been found to possess anti-inflammatory properties. See, e.g., Planta Med April 1995; 61(2):150-3 Pharmacological effects of methanolic extract from the root of Scutellaria baicalensis and its flavonoids on human gingival fibroblast. Chung C P, Park J B, Bae KH College of Dentistry, Seoul National University, Korea.

Brief Summary Text (29):
Rosemary is an antioxidant which may reduce COX-2 expression. Reference is made, e.g., Cancer Res. June 1, 1998; 58(11):2323-7 Antioxidants reduce cylooxygenase-2 expression, prostaglandin production, and proliferation in colorectal cancer cells. Chinery R, Beauchamp R D, Shyr Y, Kirkland S C, Coffey R J, Morrow JD Department of Medicine, The Vanderbilt Cancer Center, Vanderbilt University Medical Center, Nashville, Tenn. 37232, USA; J Clin Invest April 1995;95(4):1669-75 Involvement of reactive oxygen intermediates in cyclooxygenase-2 expression induced by interleukin-1, tumor necrosis factor-alpha, and lipopolysaccharide. Ferg L, Xia Y, Garcia G E, Hwang D, Wilson CB Department of Immunology, Scripps Research Instiute, La Jolla, Calif. 92037, USA.

Brief Summary Text (31):
Scutellaria baicalensis has the ability to scavenge free radicals, Reference is made, e.g., to Z Naturforsch [C] November-December 1997;52(11-12):817-23 Antioxidant activity of flavones from Scutellaria baicalensis in lecithin liposomes. Gabrielska J, Oszmianski J, Zylka R, Komorowska M Department of Physics and Biophysics, Agricultural University, Norwida, Wroclaw; and Res Commun Mol Pathol Pharmacol October 1995;90(1):103-14 Protection by baicalein against ascorbic acid-induced lipid peroxidation of rat liver microsomes. Gao D, Sakurai K, Chen J, Ogiso T Shenyang College of Pharmacy, P.R. China.

Brief Summary Text (32):
Although herbal-containing compositions for reducing inflammation are know, it is continually desirable to provide alternative herbal compositions capable of reducing inflammation, particularly by inhibiting COX-2.

Brief Summary Text (33):
Accordingly, a primary object of this invention is to provide an herbal composition capable of effectively reducing bone and joint inflammation by inhibiting COX-2.

Brief Summary Text (41):
The present invention is based on the discovery that an herbal composition composed of

specific herbs properly extracted and blended in correct proportions will safely and significantly inhibit COX-2, thereby reducing bone and joint inflammation and promoting normal cell growth.

Brief Summary Text (44):
By inhibiting COX-2, the herbal composition of this invention also promotes healthy joint function and normal cell growth.

Detailed Description Text (2):
As stated above, one aspect of the present invention provides an herbal active-ingredient composition which significantly inhibits the COX-2 enzyme, thereby reducing bone and joint inflammation.

Detailed Description Text (5):
Holy Basil (ocimum sanctum) contains the powerful COX-2 inhibitor, ursolic acid, which significantly enhances detoxification and reduces inflammation.

Detailed Description Text (6):
Turmeric contains a unique curcumin phytonutrient complex that naturally inhibits inflammatory COX-2. In addition, turmeric has been shown to possess antioxidant properties. Antioxidant activities diminish free radicals which aggravate the inflammatory response. Furthermore, recent studies have shown that tumeric is synergistic with green tea in that the presence of tumeric significantly multiplies the anti-inflammatory effect of green tea polyphenols.

Detailed Description Text (7):
Ginger inhibits both inflammatory COX-2 and 5-LOX and further functions as antioxidant. In the present invention, the ginger supercritical extract is preferably the supercritical extract of certified organic ginger.

Detailed Description Text (8):
Green tea contains polyphenols which markedly reduce COX-2. Green tea reportedly contains 51 anti-inflammatory phytonutrients.

Detailed Description Text (9):
The dual extracts of rosemary used in the present invention offer highly concentrated, full spectrum COX-2 inhibition and support detoxification.

Detailed Description Text (10):
Huzhang is the richest known source of resveratrol, which has been scientifically shown to inhibit inflammatory COX-2.

Detailed Description Text (11):
The Chinese goldthread and barberry supercritical extracts provide a unique berberine phytonutrient complex which naturally inhibits inflammatory COX-2.

Detailed Description Text (13):
Scutellariae is a unique baicalin phytonutrient complex that naturally inhibits inflammatory COX-2.

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L3: Entry 3 of 4 File: USPT May 14, 2002

DOCUMENT-IDENTIFIER: US 6387416 B1
TITLE: Anti-Inflammatory herbal composition and method of use

Brief Summary Text (11):
There are two forms of the cyclooxygenase enzyme: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). The latter form, i.e., COX-2, appears to play a key role in inflammatory processes. Recent scientific studies suggest that inhibiting the COX-2 enzyme may be an effective way to reduce inflammation without the side effects associated with irreversible COX-1 inhibition. In addition, recent scientific studies also suggest that COX-2 inhibition may serve an important function in promoting normal cell growth in the colon, pancreas, breast tissue and other organ systems.

Brief Summary Text (12):
Drugs are being developed which are intended to selectively inhibit COX-2 with minimal effect on COX-1. However, despite the emphasis on COX-2 inhibition, these drugs appear to have serious side effects, e.g., a breakdown in digestive protective mucus and prevention of normal healing processes. For example, non-steroidal anti-inflammatory drugs (NSAIDS) can have a variety of toxic side effects such as, e.g., gastric erosion and adverse effects on kidneys and liver, and may inadequately regulate the cellular immune functions and secretions of various cytokines.

Brief Summary Text (13):
Several herbs have been found to inhibit the COX-2 enzyme.

Brief Summary Text (14):
For example, holy basil has been found to possess significant anti-inflammatory properties and is capable of blocking both the cyclooxygenase and lipoxygenase pathways of arachidonate metabolism. Ursolic acid and oleanolic acid (less active), the marker constituents of holy basil, have been found to a significant COX-2 inhibitory effect.

Brief Summary Text (16):
Scutellaria baicalensis also has been found to inhibit the COX-2 enzyme.

Brief Summary Text (17):
According to the USDA database, green tea contains six constituents having cyclooxygenase-inhibitor activity. According to the Napralert database, green tea contains fifty one constituents having anti-inflammatory activity. The polyphonies in green tea were found to cause a marked reduction in cyclooxygenase-2. Flavan-3-ol derivatives (+)-catechin, also present in green tea, have been reported to be COX-1 and COX-2 inhibitors. In addition, salicylic acid, another constituent of green tea, also has been found to be a COX-2 inhibitor.

Brief Summary Text (18):
Berberine, found in barberry and Chinese goldthread, has been found to inhibit COX-2 without inhibiting COX-1 activity.

Brief Summary Text (20):
Herbs which can scavenge free radicals include, e.g., holy basil, turmeric, huzhang, oregano, and scutellaria baicalensis.

Brief Summary Text (23):

A further object of this invention is to provide the herbal composition set forth in the preceding object, wherein the composition reduces said inflammation by inhibiting COX-2.

Brief Summary Text (36):
The composition of this invention reduces inflammation by inhibiting COX-2. As a result, the composition not only reduces inflammation but also promotes healthy joint function and normal cell growth.

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L3: Entry 2 of 4 File: USPT May 21, 2002

DOCUMENT-IDENTIFIER: US 6391346 B1
TITLE: Anti-inflammatory, sleep-promoting herbal composition and method of use

Abstract Text (1):
An orally administered composition capable of reducing inflammation in animals, preferably humans, while promoting sleep for such animals, contains a therapeutically effective amount of a post-supercritical carbon dioxide hydroalcoholic extract of ginger, therapeutically effective amounts of supercritical carbon dioxide extracts of hops, chamomile, ginger, valerian and melissa; and therapeutically effective amounts of hydroalcoholic extracts of holy basil, turmeric, scutellaria baicalensis, chamomile and hops. The composition is preferably orally administered on a daily basis for at least about 4 weeks.

Brief Summary Text (11):
There are two forms of the cyclooxygenase enzyme: cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2). The latter form, i.e., COX-2, appears to play a key role in inflammatory processes. Recent scientific studies suggest that inhibiting the COX-2 enzyme may be an effective way to reduce inflammation without the side effects associated with irreversible COX-1 inhibition. In addition, recent scientific studies also suggest that COX-2 inhibition may serve an important function in promoting normal cell growth in the colon, pancreas, breast tissue and other organ systems.

Brief Summary Text (12):
Drugs are being developed which are intended to selectively inhibit COX-2 with minimal effect on COX-1. However, despite the emphasis on COX-2 inhibition, these drugs appear to have serious side effects, e.g., a breakdown in digestive protective mucus and prevention of normal healing processes. For example, non-steroidal anti-inflammatory drugs (NSAIDS) can have a variety of toxic side effects such as, e.g., gastric erosion and adverse effects on kidneys and liver, and may inadequately regulate the cellular immune functions and secretions of various cytokines.

Brief Summary Text (13):
Several herbs have been found to inhibit the COX-2 enzyme.

Brief Summary Text (14):
For example, holy basil has been found to possess significant anti-inflammatory properties and is capable of blocking both the cyclooxygenase and lipoxygenase pathways of arachidonate metabolism. Ursolic acid and oleanolic acid (less active), the marker constituents of holy basil, have been found to a significant COX-2 inhibitory effect.

Brief Summary Text (16):
Scutellaria baicalensis also has been found to inhibit the COX-2 enzyme.

Brief Summary Text (17):
According to the USDA database, green tea contains six constituents having cyclooxygenase-inhibitor activity. According to the Napralert database, green tea contains fifty one constituents having anti-inflammatory activity. The polyphenols in green tea were found to cause a marked reduction in cyclooxygenase-2. Flavan-3-ol derivatives (+)-catechin, also present in green tea, have been reported to be COX-1 and COX-2 inhibitors. In addition, salicylic acid, another constituent of green tea, also has been found to be a COX-2 inhibitor.

Brief Summary Text (18):
Berberine, found in barberry and Chinese goldthread, has been found to inhibit COX-2 without inhibiting COX-1 activity.

Brief Summary Text (20):
Herbs which can scavenge free radicals include, e.g., holy basil, turmeric, and scutellaria baicalensis.

Brief Summary Text (25):
A further object of this invention is to provide the herbal composition set forth in the preceding object, wherein the composition reduces said inflammation by inhibiting COX-2.

Brief Summary Text (33):
Accordingly, one aspect of the present invention is directed to an orally administered herbal composition capable of reducing inflammation in animals, preferably humans, afflicted with inflammation, and further capable of promoting sleep for such animals, the composition being composed of a therapeutically effective amount of a post-supercritical carbon dioxide hydroalcoholic extract of ginger; therapeutically effective amounts of supercritical carbon dioxide extracts of hops, chamomile, ginger (preferably certified organic ginger), valerian and melissa; and therapeutically effective amounts of hydroalcoholic extracts of holy basil, turmeric, scutellaria baicalensis, chamomile and hops.

Brief Summary Text (37):
The composition of this invention reduces inflammation by inhibiting COX-2. As a result, the composition not only reduces inflammation but also promotes healthy joint function and normal cell growth.

Detailed Description Text (3):
The composition of this invention is composed of: a post-supercritical carbon dioxide hydroalcoholic extract of ginger, supercritical carbon dioxide extracts of hops, chamomile, ginger (preferably certified organic ginger), valerian and melissa; and hydroalcoholic extracts of holy basil, turmeric, scutellaria baicalensis, chamomile and hops.

Detailed Description Text (4):
The composition of this invention will contain "therapeutically effective amounts" of the herbal extracts recited above. As used herein with respect to the extracts of ginger, holy basil, turmeric and scutellaria baicalensis, the term "therapeutically effective amount" refers to that amount of the extract which will contribute to the inflammation-reducing ability of the composition. With respect to the extracts of melissa, valerian, hops and chamomile, the term "therapeutically effective amount" means that amount of the herb which will promote sleep without interfering with the composition's anti-inflammatory properties. Preferably, the composition of this invention contains:

Detailed Description Text (13):
(I) from about 12% to about 18%, more preferably from about 13% to about 17%, by weight of the hydroalcoholic extract of scutellaria baicalensis;

Detailed Description Text (19):
The hydroalcoholic extracts of holy basil, turmeric, scutellaria baicalensis, hops and chamomile used in the present invention can be prepared according to conventional hydroalcoholic extraction techniques. For example, the hydroalcoholic extracts can be prepared by extracting the plant portion in a water/alcohol (preferably water/ethanol) mixture (preferably composed of 60-80 parts alcohol and 40-20 parts water), and then evaporating off the water/alcohol liquid, leaving a powdered extract residue (referred to herein as "the hydroalcoholic extract").

Detailed Description Paragraph Table (1):
TABLE Ingredient Amount Holy Basil (leaf), extract 150 mg (2% ursolic acid - 2 mg) Valerian, valeriana officinalis and 20 mg Valeriana mexicanus (root) Supercritical CO.sub.2 extract (60% valepotriates - 12 mg) Melissa (leaf) 85 mg Supercritical

CO.sub.2 extract (1% essential oil - 0.85 mg) (including neral and geranial) Turmeric (rhizome), extract 100 mg (7% curcumin - 7 mg) Scutellaria baicalensis (root), extract 5:1 100 mg Ginger (rhizome), 61.5 mg (post-supercritical CO.sub.2 ethanolic extract) (3% pungent compounds - 1.8 mg) Ginger, certified organic (rhizome) 13.5 mg Supercritical CO.sub.2 extract, (30% pungent compounds - 4 mg, 8% zingiberene - 1 mg) Chamomile (flower), supercritical CO.sub.2 extract 50 mg (minimum 25% alpha-bisabolol - 12.5 mg) Hops (strobiles), supercritical CO.sub.2 extract 50 mg (35% humulones - 17 mg) (12% lupulones - 6 mg) Hops (strobiles), ethanolic extract 25 mg (1.5% xanthohumol - 0.37 mg) Chamomile (flower), extract 25 mg (minimum 3% apigeninglycosides - 0.75 mg) Olive Oil, certified organic Yellow Beeswax

CLAIMS:

1. An orally administered composition for reducing inflammation in animals while also promoting sleep for the animals, comprising: a therapeutically effective amount of a post-supercritical carbon dioxide hydroalcoholic extract of ginger; therapeutically effective amounts of supercritical carbon dioxide extracts of hops, chamomile, ginger, valerian and melissa; and therapeutically effective amounts of hydroalcoholic extracts of holy basil, turneric, scutellaria baicalensis, chamomile and hops.

2. A composition according to claim 1, comprising:

(A) from about 7% to about 11% by weight of the post-supercritical carbon dioxide hydroalcoholic extract of ginger;

(B) from about 1% to about 3% by weight of the supercritical carbon dioxide extract of ginger;

(C) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of chamomile;

(D) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of hops;

(E) from about 18% to about 26% by weight of the hydroalcoholic extract of holy basil;

(F) from about 2.0% to about 4.0% by weight of the supercritical carbon dioxide extract of valerian;

(G) from about 10% to about 16% by weight of the supercritical carbon dioxide extract of melissa;

(H) from about 12% to about 18% by weight of the hydroalcoholic extract of turmeric;

(I) from about 12% to about 18% by weight of the hydroalcoholic extract of scutellaria baicalensis;

(J) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of chamomile; and

(K) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of hops.

3. A composition according to claim 1, comprising:

(A) from about 8% to about 10% by weight of a post-supercritical carbon dioxide hydroalcoholic extract of ginger;

(B) from about 1.5% to about 2.5% by weight of the supercritical carbon dioxide extract of ginger;

(C) from about 6% to about 8% by weight of the supercritical carbon dioxide extract of chamomile;

(D) from about 6% to about 8% by weight of the supercritical carbon dioxide extract of

hops;

(E) from about 20% to about 24% by weight of the hydroalcoholic extract of holy basil;

(F) from about 2.5% to about 3.5% by weight of the supercritical extract of valerian;

(G) from about 11% to about 15% by weight of the supercritical extract of melissa;

(H) from about 13% to about 17% by weight of the hydroalcoholic extract of turmeric;

(I) from about 13% to about 17% by weight of the hydroalcoholic extract of scutellaria baicalensis;

(J) from about 3% to about 4% by weight of the hydroalcoholic extract of chamomile; and

(K) from about 3% to about 4%, by weight of the hydroalcoholic extract of hops.

17. A composition according to claim 1, wherein the composition comprises:

(A) from about 7% to about 11% by weight of the post-supercritical carbon dioxide hydroalcoholic extract of ginger, wherein the extract comprises from about 2% to about 4% by weight of pungent compounds;

(B) from about 1% to about 3% by weight of the supercritical carbon dioxide extract of ginger, wherein the extract comprises from about 20% to about 40% by weight of pungent compounds and from about 7% to about 9% by weight of zingiberene;

(C) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of chamomile, wherein the extract comprises at least about 25% by weight of alpha-bisabolol;

(D) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of hops, wherein the extract comprises from about 30% to about 40% by weight of humulones, and from about 9% to about 15% by weight of lupulones;

(E) from about 18% to about 26% by weight of the hydroalcoholic extract of holy basil, wherein the extract comprises from about 1% to about 3% by weight of ursolic acid;

(F) from about 2.0% to about 4.0% by weight of the supercritical carbon dioxide extract of valerian, wherein the extract comprises from about 50% to about 70% by weight of valepotriates;

(G) from about 10% to about 16% by weight of the supercritical carbon dioxide extract of melissa, wherein the extract comprises from about 0.5% to about 2% by weight of essential oil;

(H) from about 12% to about 18% by weight of the hydroalcoholic extract of turmeric, wherein the extract comprises from about 5% to about 9% by weight of curcumin;

(I) from about 12% to about 18% by weight of the hydroalcoholic extract of scutellaria baicalensis;

(J) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of chamomile, wherein the extract comprises at least about 3% by weight of apigeninglycosides; and

(K) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of hops, wherein the extract comprises from about 1% to about 2% by weight of xanthohumol;

further wherein the composition comprises: (i) the post-supercritical carbon dioxide hydroalcoholic extract of ginger and the supercritical carbon dioxide extract of ginger at a weight ratio of from about 4 to about 5 parts of post-supercritical carbon dioxide hydroalcoholic extract per 1 part of supercritical carbon dioxide extract;

(ii) the supercritical carbon dioxide extract of chamomile and the hydroalcoholic extract of chamomile in a weight ratio of from about 1.75 to about 2.25 parts of the supercritical carbon dioxide extract per 1.0 part of the hydroalcoholic extract, and (ii) the supercritical carbon dioxide extract of hops and the hydroalcoholic extract of hops in a weight ratio of from about 1.75 to about 2.25 parts of the supercritical carbon dioxide extract per 1.0 part of the hydroalcoholic extract.

20. A method according to claim 19, wherein the composition provided in step (1) comprises:

(A) from about 7% to about 11% by weight of the post-supercritical carbon dioxide hydroalcoholic extract of ginger;

(B) from about 1% to about 3% by weight of the supercritical carbon dioxide extract of ginger;

(C) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of chamomile;

(D) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of hops;

(E) from about 18% to about 26% by weight of the hydroalcoholic extract of holy basil;

(F) from about 2.0% to about 4.0% by weight of the supercritical extract of valerian;

(G) from about 10% to about 16% by weight of the supercritical extract of melissa;

(H) from about 12% to about 18% by weight of the hydroalcoholic extract of turmeric;

(I) from about 12% to about 18% by weight of the hydroalcoholic extract of scutellaria baicalensis;

(J) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of chamomile; and

(K) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of hops.

21. A method according to claim 19, wherein the composition provided in step (1) comprises:

(A) from about 8% to about 10% by weight of a post-supercritical carbon dioxide hydroalcoholic extract of ginger;

(B) from about 1.5% to about 2.5% by weight of a supercritical carbon dioxide extract of ginger;

(C) from about 6% to about 8% by weight of a supercritical carbon dioxide extract of chamomile;

(D) from about 6% to about 8% by weight of a supercritical carbon dioxide extract of hops;

(E) from about 20% to about 24% by weight of the hydroalcoholic extract of holy basil;

(F) from about 2.5% to about 3.5% by weight of the supercritical extract of valerian;

(G) from about 11% to about 15% by weight of the supercritical extract of melissa;

(H) from about 13% to about 17% by weight of the hydroalcoholic extract of turmeric;

(I) from about 13% to about 17% by weight of the hydroalcoholic extract of scutellaria baicalensis;

(J) from about 3% to about 4% by weight of the hydroalcoholic extract of chamomile; and

(K) from about 3% to about 4%, by weight of the hydroalcoholic extract of hops.

35. A method according to claim 19, wherein the composition provided in step (1) comprises:

(A) from about 7% to about 11% by weight of the post-supercritical carbon dioxide hydroalcoholic extract of ginger, wherein the extract comprises from about 4% to about 6% by weight of pungent compounds;

(B) from about 1% to about 3% by weight of the supercritical carbon dioxide extract of ginger, wherein the extract comprises from about 20% to about 40% by weight of pungent compounds and from about 7% to about 9% by weight of zingiberene;

(C) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of chamomile, wherein the extract comprises at least about 25% by weight of alpha-bisabolol;

(D) from about 5.5% to about 8.5% by weight of the supercritical carbon dioxide extract of hops, wherein the extract comprises from about 30% to about 40% by weight of humulone, and from about 9% to about 15% by weight of lupulones;

(E) from about 18% to about 26% by weight of the hydroalcoholic extract of holy basil, wherein the extract comprises from about 1% to about 3% by weight of ursolic acid;

(F) from about 2.0% to about 4.0% by weight of the supercritical extract of valerian, wherein the extract comprises from about 50% to about 70% by weight of valepotriates;

(G) from about 10% to about 16% by weight of the supercritical extract of melissa, wherein the extract comprises from about 0.5 to about 2% by weight of essential oil;

(H) from about 12% to about 18% by weight of the hydroalcoholic extract of turmeric, wherein the extract comprises from about 5% to about 9% by weight of curcumin;

(I) from about 12% to about 18% by weight of the hydroalcoholic extract of scutellaria baicalensis;

(J) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of chamomile, wherein the extract comprises at least about 3% by weight of apigeninglycosides; and

(K) from about 2.5% to about 4.5% by weight of the hydroalcoholic extract of hops, wherein the extract comprises from about 1% to about 2% by weight of xanthohumol;

further wherein the composition comprises: (i) the post-supercritical carbon dioxide hydroalcoholic extract of ginger and the supercritical carbon dioxide extract of ginger at a weight ratio of from about 4 to about 5 parts of post-supercritical carbon dioxide hydroalcoholic extract per 1 part of supercritical carbon dioxide extract; (ii) the supercritical carbon dioxide extract of chamomile and the hydroalcoholic extract of chamomile in a weight ratio of from about 1.75 to about 2.25 parts of the supercritical carbon dioxide extract per 1.0 part of the hydroalcoholic extract, and (iii) the supercritical carbon dioxide extract of hops and the hydroalcoholic extract of hops in a weight ratio of from about 1.75 to about 2.25 parts of the supercritical carbon dioxide extract per 1.0 part of the hydroalcoholic extract.

WEST

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L3: Entry 1 of 4 File: USPT Nov 5, 2002

DOCUMENT-IDENTIFIER: US 6475530 B1
TITLE: Methods and compositions for producing weight loss

Abstract Text (1):
Dislcosed are methods and compositions for producing weight loss in a mammal by administration of a composition containing a weight loss effective amount of a noradrenaline stimulating compound such as ephedrine, mahuang (a plant source of ephedrine alkaloids), citrus aurantium (bitter orange), synephrine, norephedrine, psuedophedrine, a methylxanthine, such as caffeine or guarana, and a botanical COX inhibitor such as resveratrol polygonum cuspidatum, scutellaria baicalensis, turmeric, curcumin, rosmary, green tea, ocimum sanctum (holy basil), or ginger, instead of an NSAID such as aspirin, and optionally a free fatty acid reducing compound. The thermogenic formula is coupled with a growth hormone stimulating formulation containing L-arginine or L-omithine, L-lysine, and a free fatty acid reducing agent such as nicotinic acid. The thermogenic formula would preferably be administered in the daytime, and the growth hormone producing formula at nighttime. The two compositions form a system of AM and PM weight loss strategy for the therapeutic intervention of obesity.

Brief Summary Text (12):
A much safer and more effective composition for the thermogenic triad would be the use of a COX inhibitor other than aspirin. COX-2, or cyclooxygenase-2 inhibitors inhibit cyclooxygenase and reduce prostaglandins without producing the degree of gastric erosion associated with NSAID drugs such as aspirin. However, many COX-2 inhibitors have a short half-life, and do not keep prostagladins suppressed completely or in a prolonged fashion over a 6-24 hour period. In addition, the turnover rate for cyclooxygenase is fairly short.

Brief Summary Text (13):
Another attempt to formulate a weight loss product is described in U.S. Pat. No. 5798101. This patent is directed to herbal compositions to reduce weight and help suppress appetite consisting of St. John's Wort and ephedra with or without caffeine. These formulations do not include a prostaglandin inhibitor such as aspirin or a COX-2 inhibitor, so the thermogenic component (the ephedra) would be less effective at driving metabolism because of the negative feedback from prostaglandins. The St John's Wort is present to produce an effect on serotonin, a neurotransmitter involved in mood and carbohydrate craving. Thus, its function in the formulations described in this patent is as an appetite suppressant, not as a component in the thermogenic triad of ephedra, aspirin, and caffeine.

Brief Summary Text (29):
In its broadest sense, the present invention is directed to a method for producing weight loss in a mammal by administering a composition containing a weight loss effective amount of a noradrenaline stimulating compound such as ephedrine, mahuang (a plant source of ephedrine alkaloids), citrus aurantium (bitter orange), synephrine, norephedrine, psuedophedrine, a methylxanthine, such as caffeine or guarana, and a COX-2 inhibitor such as resveratrol, polygonum cuspidatum, scutellaria baicalensis, white willow bark, turmeric, curcumin, rosmary, green tea, ocimum sanctum (holy basil), or ginger, instead of an NSAID such as aspirin. The preferred COX-2 inhibitor would be resveratrol from a botanical source such as polygonum cuspidatum or polygonum multiflorum.

D Brief Summary Text (30):
Polygonum cuspidatum, a member of the buckwheat family (polygonaceae), commonly known as japanese knotweed. This plant is a native of eastern Asia, but also grows wild throughout northeastern America and southern Canada. The roots Polygonum cuspidatum contain a large amount of resveratrol, a stilbene which is a powerful anti-oxidant, and exhibits anti-inflammatory, anti-mutagen, and anti-carcinogenic properties. Resveratrol also inhibits blood platelet aggregation, making it a beneficial cardiovascular compound. Recently, resveratrol was found to inhibit COX-2 by dose dependently reducing prostaglandin,E-2 (PGE2) production in human mammary epithelial cells. The dried roots of Polygonum cuspidatum contain about 5-8% resveratrol. By using various extracting techniques to concentrate the amount of resveratrol in Polygonum cuspidatum, high yield powders have been obtained that contain up to 20% resveratrol. Therefore, 100 mg. of Polygonum cuspidatum extract will deliver 20 mg. of actual resveratrol. Synthetic resveratrol is available, but it is extremely expensive, about $250.00 per gram.

Brief Summary Text (34):
In general, the amount of ephedrine would be about 20-350 mg. per day, preferably about 25-100 mg. per day. The amount of caffeine or caffeine containing botanical yielding 10-500 mg./day, preferably about 20-200 mg./day. The amount of resveratrol or botanical source of resveratrol would yield from 1-500 mg. per day of actual resveratrol. Other COX-2 inhibitors must be used at a level that significantly inhibits the COX-2 enzyme, or enough to reduce prostaglandin synthesis sufficient to overcome feedback inhibition of the thermogenisis initiated by the noradrenaline stimulating agent. Nicotinic acid or analogues, esters, or pro-drugs of nicotininc acid may optionally be added to the thermogenic daytime formula. The components in the thermogenic triad may be in immediate-release form or sustained-release form. The ingredients are preferably in sustained-release form as this prolongs the metabolic activity and reduces the potential for side-effects that may arise from "spiking" or a rapid rise in blood levels of the respective compounds if given in immediate-release form.

Other Reference Publication (1):
Lane, N. Pain Management in Osteoarthitis: The Role of Cox-2 Inhibitors, 1997, The Journal of Rheumatology, vol. 24, Supplement 49, pp. 20-24.*

CLAIMS:

1. A weight loss composition comprising: a thermogenic noradrenaline generating substance containing at least one compound selected from the group consisting of ephedrine, synephrine and pharmaceutically acceptable salts thereof; a COX-2 inhibitor; and a methylxanthine.

2. The composition of claim 1, wherein the COX-2 inhibitor is derived from a botanical.

3. The composition of claim 2, wherein the botanical is selected from the group consisting of Polygonum cuspidatum, Polygonum multiflorum, Scutellaria baicalensis, white willow bark, turmeric, curcumin, rosemary, green tea, Ocimum sanctum (holy basil), and ginger.

5. The composition of claim 1, wherein the COX-2 inhibitor is resveratrol that is derived from Polygonum cuspidatum or Polygonum multiflorum.